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|-------------------------------|------------------------|---------------------|--|
| Notice of Allowability | Application No. | Applicant(s) | |
| | 09/461,090 | ULLRICH ET AL. | |
| | Examiner | Art Unit | |
| | FRANK W. LU | 1634 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendments filed on 4/21/2009.
2. ☒ The allowed claim(s) is/are 49.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
 - * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| <ol style="list-style-type: none"> 1. <input type="checkbox"/> Notice of References Cited (PTO-892) 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>8/07</u> 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | <ol style="list-style-type: none"> 5. <input type="checkbox"/> Notice of Informal Patent Application 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No./Mail Date <u>7/23/2009</u>. 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance 9. <input type="checkbox"/> Other _____. |
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/Frank W Lu /
Primary Examiner, Art Unit 1634

July 23, 2009

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DETAILED ACTION

Reasons for Allowance

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Monica Chin Kitts (Reg. No. 36,105) on July 23, 2009.

2. The application has been amended as follows:

Cancel claims 40-45, 47, and 48.

49. (Currently Amended) A method for modulating a G protein mediated signal transduction in in vitro comprising:

providing a cell having epidermal growth factor receptor (EGFR) comprising an extracellular domain [and having] wherein the cell has a G protein mediated signal transduction pathway [wherein] and one or more tyrosine residues on said [growth factor receptor] EGFR are phosphorylated based on the activation of the G protein mediated signal transduction pathway, the extracellular domain of said [receptor] EGFR is capable of binding to [its receptor] an EGFR ligand, and said ligand is generated from [a] the precursor of said ligand by cleavage of said precursor with a metalloproteinase from ADAM family of metalloproteinases [dependent cleavage];

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contacting said cell with a compound capable of activating said G protein mediated signal transduction pathway in the absence and presence of an inhibitor of said metalloproteinase [dependent cleavage] wherein said inhibitor blocks the release of said ligand from said precursor;

measuring tyrosine phosphorylation of said [receptor] EGFR in said cell to determine whether said G protein mediated signal transduction pathway has been activated;

comparing the levels of tyrosine phosphorylation of said [receptor] EGFR in said cell in the absence and presence of said inhibitor wherein a reduction in the level of tyrosine phosphorylation of said [receptor] EGFR in the presence of said inhibitor indicates that releasing said [receptor] EGFR ligand from said precursor is critical for activation of said G protein mediated signal transduction pathway in said cell and said activation is dependent on the interaction between the extracellular domain of said [receptor] EGFR and [its receptor] said EGFR ligand.

3. The following is an examiner's statement of reasons for allowance:

Claim 49 is allowable in light of applicant's amendments filed on April 21, 2009 and the examiner's amendments. The rejections under 35 U.S.C 112, first and second paragraph have been withdrawn in view of the examiner's amendments. The closest prior art in the record is Dong *et al.*, (Proc. Natl. Acad. Sci. USA, 96, 6235-6240, May 1999). This prior art does not teach or suggest G protein and discusses only the inhibition of autocrine signal transduction by means of EGFR (see page 12, lines 9 and 10 of applicant's brief filed on June 27, 2008). This prior art either alone or in combination with the other art in the record does/do not teach or reasonably suggest a method for modulating a G protein mediated signal transduction in *in vitro* which comprises all limitations recited in claim 49.

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Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

4. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz, can be reached on (571)272-0763.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Frank W Lu /

Primary Examiner, Art Unit 1634

July 29, 2009